2007 ATR -5 ATR G: 61	
TSCA Document Control Office (7407M)  SONNEANY SANITIZED	4
TSCA Document Control Office (7407M) ATTN: TSCA Section 8(e) Coordinator EPA East Building, Room 6428 Office of Pollution Prevention and Toxics U.S. Environmental Protection Agency 1201 Constitution Avenue, NW Washington, DC 20460-0001	
Re: TSCA 8(e) Supplemental Information to	b-chronic Toxicity
Dear Sir:  Is submitting this letter to supplement with corroborative draft clinical biochemic submission concerning draft results from an OECD 422, sub-chronic toxicity study on 1,2-Diaminocyclohexane  CASRN 694-83-7, conducted by  As discussed in our  As discussed in our  Is submission (see attachment 1), results from a 28-day toxicity study with  In drinking water, revealed a pale disconsistent of the high dose group (500 mg/kg). Pale discoloration of the liver was noted in discoloration was seen in any other dose group (0, 50, 150 mg/kg). No clear effect on live when compared to other high dose male animals which did not show pale discoloration of	gross pathology loration of livers in 5 of 10 males. No er weight was noted
when compared to other high dose male animals which did not show pale discoloration of when adjusted for body weight, an increase in liver weight was noted in all high dose male to control males. The NOEL for liver effects was 150 mg/kg.	•
when adjusted for body weight, an increase in liver weight was noted in all high dose mail	s study. Certain arding the liver aminotransferase and cholesterol
when adjusted for body weight, an increase in liver weight was noted in all high dose main to control males. The NOEL for liver effects was 150 mg/kg.	s study. Certain arding the liver aminotransferase and cholesterol o reported in high
when adjusted for body weight, an increase in liver weight was noted in all high dose main to control males. The NOEL for liver effects was 150 mg/kg.  Inas recently reviewed additional preliminary results (see Attachment 2) from this clinical biochemistry findings in this preliminary report supplement our earlier findings region discoloration described above. High serum alanine aminotransferase (ALT) and aspartate (AST) activities, as well as elevated alkaline (ALP) phosphatase (exact levels not reported) levels, were noted in the high dose male rats. High serum ALT and AST activities were also dose females, although no gross liver effects were noted.  Elevated ALT, AST, ALP, and cholesterol may be indicative of possible liver damage. Although no gross liver effects were noted.	s study. Certain arding the liver aminotransferase and cholesterol o reported in high
when adjusted for body weight, an increase in liver weight was noted in all high dose main to control males. The NOEL for liver effects was 150 mg/kg.  Th	s study. Certain arding the liver aminotransferase and cholesterol o reported in high

In order to further evaluate whether the pale discoloration and/or organ weight changes, or clinical biochemistry findings, are of toxicological relevance, microscopic examination and evaluation will be conducted. In the absence of microscopic information there is an indication that there may be a treatment-related effect on the liver in the high dose male rats.

The above information is from a draft study that has not yet been completed. Because this submitted data, as well as the previously submitted data (Attachment 1), are from a draft study, please note that there are two Laboratory Project numbers associated with these submissions, (Attachment 1) and (Attachment 2). Both Project numbers are from the same OECD 422 study and are numbered, in draft form, to reflect internal laboratory coding conventions. (Will submit the final version of the study to EPA when it becomes available.

These reports are being submitted in accordance with TSCA Section 8(e) guidance. Please do not hesitate to contact me if you have any questions. I may be reached at

Sincerely,	
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Attachments	

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## ATTACHMENT 1

8(e) Notification Letter for 1,2-Diaminocyclohexane

TRACKING Numb.	. ]	
TSCA Document Control Office (74 ATTN: TSCA Section 8(e) Coordina EPA East Building, Room 6428 Office of Pollution Prevention and U.S. Environmental Protection Age 1201 Constitution Avenue, NW Washington, DC 20460-0001	ator Toxics	
Re: TSCA 8(e) Submission for	draft Sub-chronic Toxicity data on 1	l, 2-Diaminocyclohexane
Dear Sir:		
s submitting draft results Diaminocyclohexane	s from an OECD 422, sub-chronic to CASRN 694-83-7,	xicity study on 1,2-
was noted in 5 males. No discolor effect on liver weight was noted w pale discoloration of the liver. How	reay toocity study widty:  e rats of the high dose group (500 m ration was seen in any other dose groven compared to other high dose n vever, when adjusted for body weight n compared to control males. The N	roup (0, 50, 150 mg/kg). No clear nale animals which did not show ht, an increase in liver weight was
toxicological relevance, microscopi	ner the pale discoloration and/or org ic examination and evaluation will be n indication that there may be a trea	e conducted. In the absence of
The above information is from a difinal version of the study to EPA w	raft study that has not yet been con then it becomes available.	npleted. [ ] will submit the
This report is being submitted in a contact me if you have any question	occordance with TSCA Section 8(e) gons. I may be reached at	uldance. Please do not hesitate to
Sincerely,		
Attachments	7	





## MACROSCOPIC FINDINGS MALES ALL NECROPSIES

ANIM	AL ORGAN	FINDING	DAY OF DEATH
GRO	UP 1 (CONTROL)		
1	(	No findings noted	Scheduled necropsy, 08Feb2007
2		No findings noted	Scheduled necropsy, 08Feb2007
3		No findings noted	Scheduled necropsy, 08Feb2007
4		No findings noted	Scheduled necropsy, 08Feb2007
5	Kidneys	Right side: pelvic dilation.	Scheduled necropsy, 08Feb2007
6	Bone	Tail apex: bent.	Scheduled necropsy, 08Feb2007
7		No findings noted	Scheduled necropsy, 08Feb2007
8		No findings noted	Scheduled necropsy, 08Feb2007
9		No findings noted	Scheduled necropsy, 08Feb2007
10		No findings noted	Scheduled necropsy, 08Feb2007
GRO	UP 2 (50 MG/KG)		
11	•	No findings noted	Scheduled necropsy, 08Feb2007
12		No findings noted	Scheduled necropsy, 08Feb2007
13		No findings noted	Scheduled necropsy, 08Feb2007
14		No findings noted	Scheduled necropsy, 08Feb2007
15	Bone	Tail apex: bent.	Scheduled necropsy, 08Feb2007
16		No findings noted	Scheduled necropsy, 08Feb2007
17		No findings noted	Scheduled necropsy, 08Feb2007
18		No findings noted	Scheduled necropsy, 08Feb2007
19		No findings noted	Scheduled necropsy, 08Feb2007
20	Seminal vesicles	Right side: reduced in size.	Scheduled necropsy, 08Feb2007
GRO	UP 3 (150 MG/KG)		
21		No findings noted	Scheduled necropsy, 08Feb2007
22		No findings noted	Scheduled necropsy, 08Feb2007
23		No findings noted	Scheduled necropsy, 08Feb2007
24		No findings noted	Scheduled necropsy, 08Feb2007
25		No findings noted	Scheduled necropsy, 08Feb2007
26		No findings noted	Scheduled necropsy, 08Feb2007
27		No findings noted	Scheduled necropsy, 08Feb2007
28		No findings noted	Scheduled necropsy, 08Feb2007
29		No findings noted	Scheduled necropsy, 08Feb2007
30	Seminal vesicles	Left side: reduced in size.	Scheduled necropsy, 08Feb2007
GRO	UP 4 (500 MG/KG)		
31	Liver	Discolouration, pale.	Scheduled necropsy, 08Feb2007
32		No findings noted	Scheduled necropsy, 08Feb2007
33	Liver	Discolouration, pale.	Scheduled necropsy, 08Feb2007
34		No findings noted	Scheduled necropsy, 08Feb2007
35	Liver	Discolouration, pale.	Scheduled necropsy, 08Feb2007
36	Liver	Discolouration, pale.	Scheduled necropsy, 08Feb2007
37		No findings noted	Scheduled necropsy, 08Feb2007
38		No findings noted	Scheduled necropsy, 08Feb2007
39		No findings noted	Scheduled necropsy, 08Feb2007
40	Liver	Discolouration, pale.	Scheduled necropsy, 08Feb2007





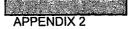


## ORGAN WEIGHTS (GRAM) MALES END OF TREATMENT

ANIMAL	BODY W. (GRAM)	BRAIN (GRAM)	HEART (GRAM)	LIVER (GRAM)	THYMUS (GRAM)	
GROUP 1	(CONTROL)					
1	451	2.03	1.348	12.08	0.619	
2	413	2.02	1.319	10.65	0.324	
3	444					
4	410	1.89	1.149	9.95	0.417	
5	421					
6	437	2.13	1.240	11.73	0.532	
7	451	2.14	1.259	12.94	0.445	
8	397					
9	380					
10	437					
GROUP 2	(50 MG/KG)					
11	453					
12	407	2.21	1.273	10.47	0.334	
13	410	2.03	1.285	10.75	0.338	
14	420	2.13	1.257	10.65	0.369	
15	381					
16	395	2.20	1.405	10.41	0.450	
17	410	2.11	1,391	9.82	0.269	
18	408					
19	422					
20	458					
GROUP 3	(150 MG/KG)					
21	411	2.25	1.389	11.26	0.405	
22	459	2.11	1.490	11.30	0.556	
23	375	1.95	1.212	9.74	0.236	
24	386	2.11	1,203	9.23	0.311	
25	464	2.01	1,447	13.12	0.386	
26	400					
27	455					
28	425					
29	396					
30	388					
GROUP 4	(500 MG/KG)					
31	412	2.15	1.405	12.49	0.242	
32	410	2.11	1.380	11.50	0.347	
33	410		~			
34	408	2.07	1.453	12.90	0.284	
35	381	2.06	1.446	12.98	0.305	
36	384	2.08	1.398	12.44	0.248	
37	391					
38	411					
39	393					
40	428					









## ORGAN WEIGHTS (GRAM) MALES END OF TREATMENT

ANIMAL	KIDNEYS (GRAM)	ADRENALS (GRAM)	SPLEEN (GRAM)	TESTES (GRAM)	EPIDIDYMIDES (GRAM)	
GROUP 1	(CONTROL)				-	
1	3.00	0.068	1.052	3.48	1.054	
2	3.29	0.070	1.096	4.51	1.448	
3				4.10	1.357	
4	2.82	0.068	0.781	3.83	1.167	
5				4.34	1.224	
6	3.17	0.046	1.219	3.92	1.181	
7	3.50	0.085	1.250	4.01	1.229	
8				4.10	1.142	
9				3.86	1.344	
10				4.25	1.353	
GROUP 2	(50 MG/KG)					
11				3.66	1.351	
12	3.20	0.067	0.937	4.14	1.187	
13	2.93	0.073	0.938	3.79	1.150	
14	2.96	0.087	0.841	3.70	1.262	
15				3.62	1.209	
16	3.00	0.058	1.086	3.60	1.290	
17	3.54	0.066	0.816	3.01	1.024	
18				3.72	1.284	
19				3.92	1.313	
20				3.78	1.199	
GROUP 3	(150 MG/KG)					
21	2.82	0.076	1.072	3.58	1.182	
22	3.63	0.064	1.084	4.18	1.248	
23	2.96	0.059	0.846	3.64	1.124	
24	2.88	0.079	0.889	3.49	1.163	
25	3.19	0.074	1.223	4.30	1.242	
26				3.86	1.074	
27				3.69	1.157	
28				3.79	1.176	
29				4.21	1.166	
30				3.70	1.158	
GROUP 4	(500 MG/KG)					
31	`3.19	0.085	0.866	3.74	1.013	
32	3.13	0.082	1.013	3.99	0.909	
33				3.97	1.058	
34	3.48	0.085	0.913	4.22	1.032	
35	3.09	0.076	0.835	3.58	1.021	
36	2.88	0.062	0.820	3.83	0.995	
37				3.87	0.886	
38				4.57	1.148	
39				3.84	1.172	
40				4.35	1.124	







# ORGAN/BODY WEIGHT RATIOS (%) MALES END OF TREATMENT

ANIMAL	BODY W. (GRAM)	BRAIN (%)	HEART (%)	LIVER (%)	THYMUS (%)					
GROUP 1	GROUP 1 (CONTROL)									
1	451	0.45	0.299	2.68	0.137					
	413	0.49	0.319	2.58	0.078					
3	444									
2 3 4	410	0.46	0.280	2.43	0.102					
5	421				<del></del>					
6	437	0.49	0.284	2.68	0.122					
7	451	0.47	0.279	2.87	0.099					
8	397	0.47	0.273	2.01	0.009					
9	380									
10	437									
	(50 MG/KG)									
11	453									
12	407	0.54	0.313	2.57	0.082					
13	410	0.49	0.313	2.62	0.082					
14	420	0.51	0.299	2.53	0.088					
15	381									
16	395	0.56	0.356	2.63	0.114					
17	410	0.51	0.339	2.39	0.066					
18	408									
19	422									
20	458									
GROUP 3	(150 MG/KG)									
21	411	0.55	0.338	2.74	0.099					
22	459	0.46	0.325	2.46	0.121					
23	375	0.52	0.323	2.60	0.063					
24	386	0.55	0.312	2.39	0.081					
25	464	0.43	0.312	2.83	0.083					
26 26	400	0.70	0.512	2.00						
20 27	455									
28	425									
29	396									
30	388									
	(500 MG/KG)	0.50	0.244	3.03	0.059					
31	412	0.52	0.341		<del>-</del>					
32	410	0.51	0.337	2.80	0.085					
33	410									
34	408	0.51	0.356	3.16	0.070					
35	381	0.54	0.380	3.41	0.080					
3 <b>6</b>	384	0.54	0.364	3.24	0.065					
37	391									
38	411									
39	3 <b>93</b>									
40	428									

APPENDIX 2

# ORGAN/BODY WEIGHT RATIOS (%) MALES END OF TREATMENT

ANIMAL	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	TESTES (%)	EPIDIDYMIDES (%)				
GROUP 1	GROUP 1 (CONTROL)								
1	0.66	0.015	0.233	0.77	0.234				
2	0.80	0.017	0.265	1.09	0.351				
3				0.92	0.306				
4	0.69	0.017	0.190	0.93	0.285				
5		U.U11		1.03	0.291				
6	0.72	0.011							
7			0.279	0.90	0.270				
	0.78	0.019	0.277	0.89	0.273				
8				1.03	0.288				
9				1.02	0.354				
10				0.97	0.310				
	(50 MG/KG)								
11				0.81	0.298				
12	0.79	0.016	0.230	1.02	0.292				
13	0.71	0.018	0.229	0.93	0.280				
14	0.70	0.021	0.200	0.88	0.300				
15				0.95	0.317				
16	0.76	0.015	0.275	0.91	0.327				
17	0.86	0.016	0.199	0.73	0.250				
18				0.91	0.315				
19				0.93	0.311				
20				0.83	0.262				
CPOUP 3	(150 MG/KG)								
21	0.69	0.018	0.261	0.87	0.288				
22	0.79	0.014	0.236	0.91	0.272				
23	0.79	0.014	0.236	0.97	0.300				
	0.79	0.020	0.226		0.301				
24				0.90					
25	0. <b>69</b>	0.016	0.264	0.93	0.268				
26				0.97	0.269				
27				0.81	0.254				
28				0.89	0.277				
29				1.06	0.294				
30				0.95	0.298				
GROUP 4	(500 MG/KG)								
31	` 0.77	0.021	0.210	0.91	0.246				
32	0.76	0.020	0.247	0.97	0.222				
33				0.97	0.258				
34	0.85	0.021	0.224	1.04	0.253				
35	0.81	0.020	0.219	0.94	0.268				
36	0.75	0.016	0.214	1.00	0.259				
37	J.7 J	J.0 10		0.99	0.227				
38				1.11	0.227				
			_	0.98	0.275				
39	_ <b></b>								
40				1.02	0.263				

ATTACHMENT 2

Clinical Biochemical Data for 1,2-Diaminocyclohexane (
From OECD 422, sub-chronic toxicity study

ATTACHMENT 2





#### INTRODUCTION

Dose Level Group 1: 0 mg/kg body weight (Milli-U water)

Group 2: 50 mg/kg body weight Group 3: 150 mg/kg body weight Group 4 500 mg/kg body weight

The purpose of this study was to evaluate the potential toxic effects of the test substance when administered to rats for a minimum of 28 days and to evaluate the potential of the test substance to affect male and female reproductive performance such as gonadal function, mating behaviour, conception, parturition and early postnatal development.

#### **MATERIALS AND METHODS**

#### **Allocation**

Group	Dose level	Number of animals		Animals numbers	
,	mg/kg b.w./day	F <sub>0</sub> males	F <sub>0</sub> females	males	females
1	0	10	10	01-10	41-50
2	50	10	10	11-20	51-60
3	150	10	10	21-30	61-70
4	500	10	10	31-40	71-80

#### **RESULTS**

#### Mortality

One animal treated at 50 mg/kg (Female 60) was sacrificed due to cannibalism of the pups. One female at 500 mg/kg (Female 79) was sacrificed due to litter loss on Day 2 of lactation. This animal had five pups, three pups were found dead on Day 1 of lactation, two other pups were found dead on Day 2 of lactation.

#### Clinical signs

Slight to moderate salivation was noted in all males and females treated at 500 mg/kg. Furthermore, incidentally rales was noted in two males at 500 mg/kg (Males 37 and 38) and piloerection was noted in one female at 500 mg/kg (Female 79) at the end of treatment.

Yellow discolouration of the urine was noted in all animals of Groups 2, 3 and 4 in a dose dependant manner.

Other clinical signs (scabs, chromodacryorrhoea, broken tail apex, diarrhoea and alopecia) were considered unrelated to treatment.

#### **Body weight**

Reduced body weight gain was noted in males treated at 500 mg/kg during premating and mating. Reduced body weight and body weight gain was also noted in females treated at 500 mg/kg on Days 14 to 20 *post-coitum* and during lactation (not always statistically significant).

#### **Food consumption**

Food consumption before or after allowance for body weight was reduced during lactation in females treated at 500 mg/kg (statistically not significant).

Other changes in food consumption were considered to be of no toxicological relevance.

#### **Functional observations**

No effects were noted at functional observations.

Results on the motor activity test will be added in the draft report.





Haematology

A slight increase in red blood cell distribution width was noted in males at 500 mg/kg. A decrease in eosinophils was noted in females at 500 mg/kg.

Other findings achieving statistical significance (increased APTT in males at 50 and 150 mg/kg) were considered to be of no toxicological relevance in absence of a dose response relationship.

Clinical biochemistry

Treatment related effects were mainly noted in males treated at 500 mg/kg. These findings comprised high alanine aminotransferase and aspartate aminotransferase activities (also noted in females at 500 mg/kg) and increased ALP and cholesterol levels. Cholesterol levels were also increased in males treated at 150 mg/kg, but to a lesser extent.

Furthermore, calcium levels were increased in males and females at 500 mg/kg.

Other findings achieving statistical significance (decreased potassium levels in males at 50 mg/kg and increased albumin in females at 150 mg/kg) were considered to be of no toxicological relevance in absence of a dose response relationship.

**Macroscopic examination** 

Pale discolouration of the liver was noted in five males treated at 500 mg/kg. No other treatment related effects were noted.

One female at 50 mg/kg (Female 51) showed an enlarged cervix and uterus. The uterus was filled with fluid. These are signs of pseudo pregnancy. These findings were considered to be unrelated to treatment.

Incidental findings among control and treated animals included an enlarged adrenal gland, pelvic dilation of the kidney, reduced size of the seminal vesicles, bent tail apex (correlating to the broken tail apex noted at clinical observations), alopecia, foci on the lungs and diaphragmatic hernia of the liver. These findings are occasionally seen among rats used in these types of study and/or in the absence of a dose response relationship they were considered changes of no toxicological significance.

Organ weights

Liver/body weight ratios were increased with statistical significance for males treated at 500 mg/kg. In addition, thymus/body weight ratios were decreased with statistical significance for males and females treated at 500 mg/kg.

Other changes in organ weight comprised decreased spleen weight in males and females at 500 mg/kg (not always statistically significant), increased heart weight in males at 50, 150 and 500 mg/kg and females at 500 mg/kg, decreased epididymides weight in males at 500 mg/kg, increased relative brain weight in males at 500 mg/kg, increased kidney weight in females at 500 mg/kg and increased adrenal weight in females at 150 and 500 mg/kg.

Other changes (increased liver weight in females at 50 mg/kg, decreased testes weight in males at 50 mg/kg) were considered to be of no toxicological relevance in absence of a dose response relationship.





#### Maternal reproduction data

No effect was noted on the duration of gestation and precoital time at 50, 150 or 500 mg/kg.

Five females were non-pregnant (one in the control group, one in the low dose group and three in the high dose group).

One animal treated at 50 mg/kg (Female 60) was sacrificed due to cannibalism of all pups. One female at 500 mg/kg (Female 79) showed total litter loss.

Erroneously, one female treated at 50 mg/kg (Female 55) was sacrificed before the end of gestation. This female was found to be pregnant. Details will be added in the report.

#### Litter size/viability of pups

At the first litter check, the average and total number of living pups per litter was reduced at 500 mg/kg (average of 6.9 pups per litter) when compared to concurrent controls (average of 16.0 pups per litter).

Increased postnatal loss was noted at 150 and 500 mg/kg, resulting in a reduced viability index. At 150 mg/kg, postnatal loss was noted in animals 62 (1 of 14 pups), 63 (2 of 20 pups), 67 (1 of 17 pups), 68 (4 of 17 pups) and 69 (2 of 18 pups). At 500 mg/kg, postnatal loss was noted in animals 78 (8 of 11 pups) and 79 (5 of 5 pups).

Increased postnatal loss was also noted at 50 mg/kg. This was mainly due to one animal (Female 60) who cannibalized the pups (in total 13 pups). This was considered to be unrelated to treatment, as no such behaviour was noted in mid and high dose group.

#### Sex ratios

No treatment related effect on the sex ratio was noted.

#### Foetal body weight

No treatment related effect on body weights of fetuses was noted.

Please note: For a proper evaluation all in-life data and pathology data are required, therefore the above mentioned findings are preliminary and indicative.

Public Version	
TRACKING Number:	
TSCA Document Control Office (7407M) ATTN: TSCA Section 8(e) Coordinator EPA East Building, Room 6428 Office of Pollution Prevention and Toxics U.S. Environmental Protection Agency 1201 Constitution Avenue, NW Washington, DC 20460-0001	
Re: TSCA 8(e) Supplemental Information to Clinical Biochemistry Data on 1,2-Diaminocyclohexane	: Draft Corroborative Sub-chronic Toxicity
Dear Sir:	
is submitting this letter to supplement with corroborative submission concerning draft results from an OECD 422, sub-chrobiaminocyclohexane CASRN 694-83-7, conducted by	nic toxicity study on 1,2-
As discussed in our submission a 28-day toxicity study with in drinking wat male rats of the high dose group (500 mg/kg). Pale discoloration discoloration was seen in any other dose group (0, 50, 150 mg/kg) when compared to other high dose male animals which did not swhen adjusted for body weight, an increase in liver weight was not control males. The NOEL for liver effects was 150 mg/kg.	of the liver was noted in 5 of 10 males. No g). No clear effect on liver weight was noted how pale discoloration of the liver. However,
thas recently reviewed additional preliminary results (see clinical biochemistry findings in this preliminary report supplement discoloration described above. High serum alanine aminotransfer (AST) activities, as well as elevated alkaline (ALP) phosphatase (elevels, were noted in the high dose male rats. High serum ALT and dose females, although no gross liver effects were noted.	at our earlier findings regarding the liver rase (ALT) and aspartate aminotransferase exact levels not reported) and cholesterol
Elevated SIT ACT SID and chalastered may be indicative of according	rible liver demans. Although bischessical

In order to further evaluate whether the pale discoloration and/or organ weight changes, or clinical biochemistry findings, are of toxicological relevance, microscopic examination and evaluation will be conducted. In the absence of microscopic information there is an indication that there may be a treatment-related effect on the liver in the high dose male rats.

The above information is from a draft study that has not yet been completed. Because this submitted data, as well as the previously submitted data (Attachment 1), are from a draft study, please note that there are two Laboratory Project numbers associated with these submissions, (Attachment 1) and (Attachment 2). Both Project numbers are from the same OECD 422 study and are numbered, in draft form, to reflect internal laboratory coding conventions. (Will submit the final version of the study to EPA when it becomes available.

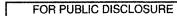
These reports are being submitted in accordance with TSCA Section 8(e) guidance. Please do not hesitate to contact me if you have any questions. I may be reached at

Sincerely,	
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Attachments	

## ATTACHMENT 1

8(e) Notification Letter for 1,2-Diaminocyclohexane

TRACK	ang Numb	•			
[	7	-			
ATTN: EPA E: Office U.S. E: 1201 (	Document Control Offi : TSCA Section 8(e) Co ast Building, Room 64: of Pollution Prevention invironmental Protection Constitution Avenue, North 1986, DC 20460-000	ordinator 28 n and Toxics on Agency IW			
Re:	TSCA 8(e) Submissi	on for draft Sub-chro	onic Toxicity data o	n 1,2-Diaminocy	clohexane
Dear S	Sir:				
Diamir	is submitting draft nocyclohexand (	results from an OEC CASRN	D 422, sub-chronic 694-83-7,	_	-
pale di was no effect pale di	pathology results from iscoloration of itvers in oted in 5 males. No d on liver weight was no iscoloration of the live in all high dose males	n male rats of the high iscoloration was seen sted when compared r. However, when ac	gh dose group (500 in in any other dose I to other high dose djusted for body we	mg/kg). Pale di group (0, 50, 1 male animals w glght, an increase	50 mg/kg). No clear hich did not show e in liver weight was
toxicol micros	er to further evaluate logical relevance, micro scopic information ther gh dose male rats.	oscopic examination	and evaluation will	be conducted.	In the absence of
	pove information is fro ersion of the study to i			ompleted.	]will submit the
	eport is being submitte t me if you have any o			guidance. Pleas	se do not hesitate to
Sincere	ety,				
Attachn	ments				







## MACROSCOPIC FINDINGS MALES ALL NECROPSIES

ANIM	AL ORGAN	FINDING	DAY OF DEATH
GRO	UP 1 (CONTROL)		
1	,	No findings noted	Scheduled necropsy, 08Feb2007
2		No findings noted	Scheduled necropsy, 08Feb2007
3		No findings noted	Scheduled necropsy, 08Feb2007
4		No findings noted	Scheduled necropsy, 08Feb2007
5	Kidneys	Right side: pelvic dilation.	Scheduled necropsy, 08Feb2007
6	Bone	Tail apex: bent.	Scheduled necropsy, 08Feb2007
7		No findings noted	Scheduled necropsy, 08Feb2007
8		No findings noted	Scheduled necropsy, 08Feb2007
9		No findings noted	Scheduled necropsy, 08Feb2007
10		No findings noted	Scheduled necropsy, 08Feb2007
GRO	UP 2 (50 MG/KG)		
11	•	No findings noted	Scheduled necropsy, 08Feb2007
12		No findings noted	Scheduled necropsy, 08Feb2007
13		No findings noted	Scheduled necropsy, 08Feb2007
14		No findings noted	Scheduled necropsy, 08Feb2007
15	Bone	Tail apex: bent.	Scheduled necropsy, 08Feb2007
16		No findings noted	Scheduled necropsy, 08Feb2007
17		No findings noted	Scheduled necropsy, 08Feb2007
18		No findings noted	Scheduled necropsy, 08Feb2007
19		No findings noted	Scheduled necropsy, 08Feb2007
20	Seminal vesicles	Right side: reduced in size.	Scheduled necropsy, 08Feb2007
GRO	UP 3 (150 MG/KG)		
21		No findings noted	Scheduled necropsy, 08Feb2007
22		No findings noted	Scheduled necropsy, 08Feb2007
23		No findings noted	Scheduled necropsy, 08Feb2007
24		No findings noted	Scheduled necropsy, 08Feb2007
25		No findings noted	Scheduled necropsy, 08Feb2007
26		No findings noted	Scheduled necropsy, 08Feb2007
27		No findings noted	Scheduled necropsy, 08Feb2007
28		No findings noted	Scheduled necropsy, 08Feb2007
29		No findings noted	Scheduled necropsy, 08Feb2007
30	Seminal vesicles	Left side: reduced in size.	Scheduled necropsy, 08Feb2007
	UP 4 (500 MG/KG)		
31	Liver	Discolouration, pale.	Scheduled necropsy, 08Feb2007
32		No findings noted	Scheduled necropsy, 08Feb2007
33	Liver	Discolouration, pale.	Scheduled necropsy, 08Feb2007
34		No findings noted	Scheduled necropsy, 08Feb2007
35	Liver	Discolouration, pale.	Scheduled necropsy, 08Feb2007
36	Liver	Discolouration, pale.	Scheduled necropsy, 08Feb2007
37		No findings noted	Scheduled necropsy, 08Feb2007
38		No findings noted	Scheduled necropsy, 08Feb2007
39		No findings noted	Scheduled necropsy, 08Feb2007
40	Liver	Discolouration, pale.	Scheduled necropsy, 08Feb2007







## ORGAN WEIGHTS (GRAM) MALES END OF TREATMENT

ANIMAL	BODY W. (GRAM)	BRAIN (GRAM)	HEART (GRAM)	LIVER (GRAM)	THYMUS (GRAM)	
GROUP 1	(CONTROL)					
1	451	2.03	1.348	12.08	0.619	
2	413	2.02	1.319	10.65	0.324	
3	444					
4	410	1.89	1.149	9.95	0.417	
5	421					
6	437	2.13	1.240	11.73	0.532	
7	451	2.14	1.259	12.94	0.445	
8	397				~~~	
9	380					
10	437					
	(50 MG/KG)					
11	453		4.070	40.47	2004	
12	407	2.21	1.273	10.47	0.334	
13	410	2.03	1.285	10.75	0.338	
14	420	2.13	1.257	10.65	0.369	
15	381					
16	395	2.20	1.405	10.41	0.450	
17	410	2.11	1.391	9.82	0.269	
18	408					
19	422					
20	458					
GROUP 3	(150 MG/KG)					
21	411	2.25	1.389	11.26	0.405	
22	459	2.11	1.490	11.30	0.556	
23	375	1.95	1.212	9.74	0.236	
24	386	2.11	1.203	9.23	0.311	
25	464	2.01	1,447	13.12	0.386	
26	400					
27	455					
28	425					
29	396					
30	388					
	(500 MG/KG)	2.45	4.405	10.40	0.040	
31	412	2.15	1.405	12.49	0.242	
32	410	2.11	1.380	11.50	0.347	
33	410			40.00		
34	408	2.07	1.453	12.90	0.284	
35	381	2.06	1.446	12.98	0.305	
36	384	2.08	1.398	12.44	0.248	
37	391					
38	411					
39	393					
40	428					







## ORGAN WEIGHTS (GRAM) MALES END OF TREATMENT

ANIMAL	KIDNEYS (GRAM)	ADRENALS (GRAM)	SPLEEN (GRAM)	TESTES (GRAM)	EPIDIDYMIDES (GRAM)
GROUP 1	(CONTROL)				
1	3.00	0.068	1.052	3.48	1.054
2	3.29	0.070	1.096	4.51	1.448
3				4.10	1.357
4	2.82	0.068	0.781	3.83	1.167
5				4.34	1.224
6	3.17	0.046	1.219	3.92	1.181
7	3.50	0.085	1.250	4.01	1.229
8				4.10	1.142
9				3.86	1.344
10				4.25	1.353
				7.20	1.500
	(50 MG/KG)				
11				3.66	1.351
12	3.20	0.067	0.937	4.14	1.187
13	2.93	0.073	0.938	3.79	1.150
14	2.96	0.087	0.841	3.70	1.262
15				3.62	1.209
16	3.00	0.058	1.086	3.60	1.290
17	3.54	0.066	0.816	3.01	1.024
18				3.72	1.284
19	~			3.92	1.313
20				3.78	1.199
GROUP 3	(150 MG/KG)				
21	2.82	0.076	1.072	3.58	1.182
22	3.63	0.064	1.084	4.18	1.248
23	2.96	0.059	0.846	3.64	1.124
24	2.88	0.079	0.889	3.49	1.163
25	3.19	0.074	1.223	4.30	1.242
26	~			3.86	1.074
27				3.69	1.157
28				3.79	1.176
29				4.21	1.166
30				3.70	1.158
GROUP 4	(500 MG/KG)				
31	3.19	0.085	0.866	3.74	1.013
32	3.13	0.082	1.013	3.99	0.909
33				3.97	1.058
34	3.48	0.085	0.913	4.22	1.032
35	3.09	0.076	0.835	3.58	1.021
36	2.88	0.062	0.820	3.83	0.995
37				3.87	0.886
38	~			4.57	1.148
39				3.84	1.172
40				4.35	1.124







# ORGAN/BODY WEIGHT RATIOS (%) MALES END OF TREATMENT

ANIMAL	BODY W. (GRAM)	BRAIN (%)	HEART (%)	LIVER (%)	THYMUS (%)	
GROUP 1	(CONTROL)					
1	`451	0.45	0.299	2.68	0.137	
2	413	0.49	0.319	2.58	0.078	
3	444			******		
4	410	0.46	0.280	2.43	0.102	
5	421					
6	437	0.49	0.284	2.68	0.122	
7	451	0.47	0.279	2.87	0.099	
8	397					
9	380					
10	437					
,,,	107					
	(50 MG/KG)					
11	453					
12	407	0.54	0.313	2.57	0.082	
13	410	0.49	0.313	2.62	0.082	
14	420	0.51	0.299	2.53	0.088	
15	381					
16	395	0.56	0.356	2.63	0.114	
17	410	0.51	0.339	2.39	0.066	
18	408					
19	422					
20	458					
GROUP 3	(150 MG/KG)					
21	` 411	0.55	0.338	2.74	0.099	
22	459	0.46	0.325	2.46	0.121	
23	375	0.52	0.323	2.60	0.063	
24	386	0.55	0.312	2.39	0.081	
25	464	0.43	0.312	2.83	0.083	
26	400					
27	455					
28	425					
29	396					
30	388					
GROUP 4	(500 MG/KG)					
31	412	0.52	0.341	3.03	0.059	
32	410	0.51	0.337	2.80	0.085	
33	410					
34	408	0.51	0.356	3.16	0.070	
35	381	0.54	0.380	3.41	0.080	
36	384	0.54	0.364	3.24	0.065	
37	391					
38	411					
39	393					
40	428					



APPENDIX 2

# ORGAN/BODY WEIGHT RATIOS (%) MALES END OF TREATMENT

ANIMAL	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	TESTES (%)	EPIDIDYMIDES (%)
GROUP 1	(CONTROL)				
1	0.66	0.015	0.233	0.77	0.234
2	0.80	0.017	0.265	1.09	0.351
3				0.92	0.306
4	0.69	0.017	0.190	0.93	0.285
5				1.03	0.291
6	0.72	0.011	0.279	0.90	0.270
7	0.78	0.019	0.277	0.89	0.273
8				1.03	0.288
9				1.02	0.354
10				0.97	0.310
GROUP 2	(50 MG/KG)			0.81	0.298
12	0.79	0.016	0.230	1.02	0.292
13	0.71	0.018	0.229	0.93	0.280
14	0.70	0.021	0.200	0.88	0.300
15	0.70 	0.02 1	0.200	0.95	0.317
16	0.76	0.015	0.275	0.91	0.317
17	0.86	0.016	0.199	0.73	0.250
18	0.00	0.010	0.199	0.73	0.230
19				0.93	0.313
20				0.83	0.262
				0.00	0.202
	(150 MG/KG)				
21	0.69	0.018	0.261	0.87	0.288
22	0.79	0.014	0.236	0.91	0.272
23	0.79	0.016	0.226	0.97	0.300
24	0.75	0.020	0.230	0.90	0.301
25	0.6 <del>9</del>	0.016	0.264	0.93	0.268
26				0.97	0.269
27				0.81	0.254
28				0.89	0.277
29				1.06	0.294
30				0.95	0.298
	(500 MG/KG)				
31	0.77	0.021	0.210	0.91	0.246
32	0.76	0.020	0.247	0.97	0.222
33				0.97	0.258
34	0.85	0.021	0.224	1.04	0.253
35	0.81	0.020	0.219	0.94	0.268
36	0.75	0.016	0.214	1.00	0.259
37				0.99	0.227
38				1.11	0.279
39				0.98	0.298
40				1.02	0.263

\* 1 , 1 %

ATTACHMENT 2
Clinical Biochemical Data for 1,2-Diaminocyclohexane (
From OECD 422, sub-chronic toxicity study

ATTACHMENT 2





#### INTRODUCTION

Dose Level

Group 1: 0 mg/kg body weight (Milli-U water)

Group 2: 50 mg/kg body weight Group 3: 150 mg/kg body weight Group 4 500 mg/kg body weight

The purpose of this study was to evaluate the potential toxic effects of the test substance when administered to rats for a minimum of 28 days and to evaluate the potential of the test substance to affect male and female reproductive performance such as gonadal function, mating behaviour, conception, parturition and early postnatal development.

#### **MATERIALS AND METHODS**

#### Allocation

Group	Dose level	Number	of animals	Animals numbers	
	mg/kg b.w./day	F <sub>0</sub> males	F <sub>0</sub> females	males	females
1	0	10	10	01-10	41-50
2	50	10	10	11-20	51-60
3	150	10	10	21-30	61-70
4	500	10	10	31-40	71-80

### RESULTS

#### Mortality

One animal treated at 50 mg/kg (Female 60) was sacrificed due to cannibalism of the pups. One female at 500 mg/kg (Female 79) was sacrificed due to litter loss on Day 2 of lactation. This animal had five pups, three pups were found dead on Day 1 of lactation, two other pups were found dead on Day 2 of lactation.

#### Clinical signs

Slight to moderate salivation was noted in all males and females treated at 500 mg/kg. Furthermore, incidentally rales was noted in two males at 500 mg/kg (Males 37 and 38) and piloerection was noted in one female at 500 mg/kg (Female 79) at the end of treatment.

Yellow discolouration of the urine was noted in all animals of Groups 2, 3 and 4 in a dose dependant manner.

Other clinical signs (scabs, chromodacryorrhoea, broken tail apex, diarrhoea and alopecia) were considered unrelated to treatment.

#### **Body weight**

Reduced body weight gain was noted in males treated at 500 mg/kg during premating and mating. Reduced body weight and body weight gain was also noted in females treated at 500 mg/kg on Days 14 to 20 post-coitum and during lactation (not always statistically significant).

## Food consumption

Food consumption before or after allowance for body weight was reduced during lactation in females treated at 500 mg/kg (statistically not significant).

Other changes in food consumption were considered to be of no toxicological relevance.

#### **Functional observations**

No effects were noted at functional observations.

Results on the motor activity test will be added in the draft report.





Haematology

A slight increase in red blood cell distribution width was noted in males at 500 mg/kg. A decrease in eosinophils was noted in females at 500 mg/kg.

Other findings achieving statistical significance (increased APTT in males at 50 and 150 mg/kg) were considered to be of no toxicological relevance in absence of a dose response relationship.

Clinical biochemistry

Treatment related effects were mainly noted in males treated at 500 mg/kg. These findings comprised high alanine aminotransferase and aspartate aminotransferase activities (also noted in females at 500 mg/kg) and increased ALP and cholesterol levels. Cholesterol levels were also increased in males treated at 150 mg/kg, but to a lesser extent.

Furthermore, calcium levels were increased in males and females at 500 mg/kg.

Other findings achieving statistical significance (decreased potassium levels in males at 50 mg/kg and increased albumin in females at 150 mg/kg) were considered to be of no toxicological relevance in absence of a dose response relationship.

**Macroscopic examination** 

Pale discolouration of the liver was noted in five males treated at 500 mg/kg. No other treatment related effects were noted.

One female at 50 mg/kg (Female 51) showed an enlarged cervix and uterus. The uterus was filled with fluid. These are signs of pseudo pregnancy. These findings were considered to be unrelated to treatment.

Incidental findings among control and treated animals included an enlarged adrenal gland, pelvic dilation of the kidney, reduced size of the seminal vesicles, bent tail apex (correlating to the broken tail apex noted at clinical observations), alopecia, foci on the lungs and diaphragmatic hernia of the liver. These findings are occasionally seen among rats used in these types of study and/or in the absence of a dose response relationship they were considered changes of no toxicological significance.

Organ weights

Liver/body weight ratios were increased with statistical significance for males treated at 500 mg/kg. In addition, thymus/body weight ratios were decreased with statistical significance for males and females treated at 500 mg/kg.

Other changes in organ weight comprised decreased spleen weight in males and females at 500 mg/kg (not always statistically significant), increased heart weight in males at 50, 150 and 500 mg/kg and females at 500 mg/kg, decreased epididymides weight in males at 500 mg/kg, increased relative brain weight in males at 500 mg/kg, increased kidney weight in females at 500 mg/kg and increased adrenal weight in females at 150 and 500 mg/kg.

Other changes (increased liver weight in females at 50 mg/kg, decreased testes weight in males at 50 mg/kg) were considered to be of no toxicological relevance in absence of a dose response relationship.





Maternal reproduction data

No effect was noted on the duration of gestation and precoital time at 50, 150 or 500 mg/kg.

Five females were non-pregnant (one in the control group, one in the low dose group and three in the high dose group).

One animal treated at 50 mg/kg (Female 60) was sacrificed due to cannibalism of all pups. One female at 500 mg/kg (Female 79) showed total litter loss.

Erroneously, one female treated at 50 mg/kg (Female 55) was sacrificed before the end of gestation. This female was found to be pregnant. Details will be added in the report.

Litter size/viability of pups

At the first litter check, the average and total number of living pups per litter was reduced at 500 mg/kg (average of 6.9 pups per litter) when compared to concurrent controls (average of 16.0 pups per litter).

Increased postnatal loss was noted at 150 and 500 mg/kg, resulting in a reduced viability index. At 150 mg/kg, postnatal loss was noted in animals 62 (1 of 14 pups), 63 (2 of 20 pups), 67 (1 of 17 pups), 68 (4 of 17 pups) and 69 (2 of 18 pups). At 500 mg/kg, postnatal loss was noted in animals 78 (8 of 11 pups) and 79 (5 of 5 pups).

Increased postnatal loss was also noted at 50 mg/kg. This was mainly due to one animal (Female 60) who cannibalized the pups (in total 13 pups). This was considered to be unrelated to treatment, as no such behaviour was noted in mid and high dose group.

#### Sex ratios

No treatment related effect on the sex ratio was noted.

#### Foetal body weight

No treatment related effect on body weights of fetuses was noted.

Please note: For a proper evaluation all in-life data and pathology data are required, therefore the above mentioned findings are preliminary and indicative.

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Certified Mail TRACKING Number:

C711117 -7 AMIL: 01

TSCA Document Control Office (7407M)
ATTN: Bernice Mudd
TSCA Section 8(e) Coordinator
EPA East Building, Room 6428
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
1201 Constitution Avenue, NW
Washington, DC 20460-0001

Re: 8EHQ-07-16749 – Substantiation of Confidentiality

Dear Ms. Mudd:

As discussed in our telephone conversation last week, I have enclosed the TSCA CBI substantiation documentation for the 8(e) submissions for 1,2-Diaminocyclohexane, referenced by 8EHQ-07-16749. The enclosed documents include:

1. A marked version of the

8(e) Notification for 1,2-Diaminocyclohexane.

2. Two sanitized copies of the

8(e) Notification for 1,2-Diaminocyclohexane.

3. A marked version of the

8(e) Supplemental Notification for 1,2-Diaminocyclohexane.

4. Two sanitized copies of the

8(e) Supplemental Notification for 1,2-Diaminocyclohexane.

- 5. Support Information for Confidentiality Claims for 8EHQ-07-16749.
- 6. Two sanitized copies of the Support Information for Confidentiality Claims for 8EHQ-07-16749.
- 7. Two sanitized copies of this letter.

This information is being submitted in accordance with TSCA Section 8(e) guidance. Please do not hesitate to contact me if you have any questions. I may be reached at

Sincerely,

Attachments

## **Support Information for Confidentiality Claims**

1. Is your company asserting this confidential business information (CBI) claim on its own behalf? If the answer is no, please provide company name, address and telephone number of entity asserting claim.

is asserting this CBI claim on its own behalf.

2. For what period do you assert your claim(s) of confidentiality? If the claim is to extend until a certain event or point in time, please indicate that event or time period. Explain why such information should remain confidential until such point.

The information of the study report being claimed as CBI should be held confidential indefinitely.

3. Has the information that you are claiming as confidential been disclosed to any other governmental agency, or to this Agency at any other time? Identify the Agency to which the information was disclosed and provide the date and circumstances of the same. Was the disclosure accompanied by a claim of confidentiality? If yes, attach a copy of said document reflecting the confidentiality agreement.

The report has not been disclosed to any other agency. It is possible that a robust summary of the study data, not including the information claimed as CBI, could be used in High Production Volume program submittals.

4. Briefly describe any physical or procedural restrictions within your company relating to the use and storage of the information you are claiming CBI.

Access to the building where the Study Report is housed is restricted to employees and to guests who are escorted by an employee. An electronic version of the report is stored on a password-protected data server. Access to that server requires approval from the IT department as well as the Director of Environmental, Health and Safety.

5. If anyone outside your company has access to any of the information claimed CBI, are they restricted by confidentiality agreement(s). If so, explain the content of the agreement(s).

The entities outside who have access to the Study Report are restricted by confidentiality agreements with . These entities include the performing laboratory itself, a 3<sup>rd</sup> party consultant under contract to to assist with the final data review and outside legal counsel which provides legal assistance and review of any submissions to a government agency.

's contract with the testing laboratory states:

All Studies, Study Protocols and other information developed for by Laboratory in connection with the Work performed hereunder, the existence and conduct of any

discussion between the Parties, and the terms of this Agreement, shall also constitute Confidential Information . . . 's Confidential Information shall be held in strictest confidence by Laboratory and shall be used solely for purposes of performing the Work. Laboratory shall not disclose any of 's Confidential Information to anyone...

's Services Agreement with the 3<sup>rd</sup> party consultant states:

The consultant shall "hold so Proprietary Information in strictest confidence, shall not disclose it to others, shall use it solely for purposes of performing such Service, and shall upon so request, deliver to solely for purposes of performing such Service, and shall upon so request, deliver to solely for purposes of performing such Service, and shall upon solely for purposes of performance such services and shall upon solely for purposes of performance solely for p

- 6. Does the information claimed as confidential appear or is it referred to in any of the following:
  - a. Advertising or promotional material for the chemical substance or the resulting and product:
  - b. Material safety data sheets or other similar materials (such as technical data sheets) for the substance or resulting end product (include copies of this information as it appears when accompanying the substance and/or product at the time of transfer or sale);
  - c. Professional or trade publications; or
  - d. Any other media or publications available to the public or to your competitors. If you answered yes to any of the above, indicate where the information appears, include copies, and explain why it should nonetheless be treated as confidential.

While the *results* of the study will appear on Material Safety Data Sheets, the information claimed as confidential does not and will not appear in any of the materials listed above.

7. Has EPA, another federal agency, or court made any confidentiality determination regarding information associated with this substance? If so, provide copies of such determinations.

No.

8. Describe the substantial harmful effects that would result to your competitive position if the CBI information is made available to the public? In your answer, explain the causal relationship between disclosure and any resulting substantial harmful effects. Consider in your answer such constraints as capital and marketing cost, specialized technical expertise, or unusual processes and your competitors access to your customers. Address each piece of information claimed CBI separately.

A competitor, upon having easily obtainable access to the association between the company, the commercial product name identified in the study and the study details could use this information to their commercial advantage in an attempt to position an alternative to the product in the marketplace.

9. Has the substance been patented in the U.S. or elsewhere? Is a patent for the substance currently pending?

No patent application has been filed for this substance.

- 10. Is this substance/product commercially available and if so, for how long has it been available on the commercial market?
  - a. If on the commercial market, are your competitors aware that the substance is commercially available in the U.S.?
  - b. If not already commercially available, describe what stage of research and development (R&D) the substance is in, and estimate bow soon a market will be established.
  - c. What is the substance used for and what type of product(s) does it appear in.

is currently sold in the US and the EU as an intermediate for use in manufacture of curing agents for epoxy resins and chain extenders for polyurethanes. has been on the commercial market for approximately 20 years. Competitors would be aware that the substance is commercially available.

11. Describe whether a competitor could employ reverse engineering to identically recreate the substance?

Yes.

- 12. Do you assert that disclosure of this information you are claiming CBI would reveal:
  - a. confidential processes used in manufacturing the substance;

No

- b. if a mixture, the actual portions of the substance in the mixture; or
- c. information unrelated to the effects of the substance on human health or the environment?

Yes

If your answer to any of the above questions is yes, explain how such information would be revealed.

It would reveal the company name, the commercial product name and the testing laboratory associated with the preliminary test report data being submitted for the chemical substance.

13. Provide the Chemical Abstract Service Registry Number for the product, if known. Is your company applying for a CAS number now or in the near future? If you have applied for a CAS number, include a copy of the contract with CAS.

The CAS Registry Number is 694-83-7.

14. Is the substance or any information claimed CBI the subject of FIFRA regulation or reporting? If so, explain.

No.

RECEIVED

Certified Mail TRACKING Number:

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TSCA Document Control Office (7407M)
ATTN: Bernice Mudd
TSCA Section 8(e) Coordinator
EPA East Building, Room 6428
Office of Pollution Prevention and Toxics
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4. Two sanitized copies of the

8(e) Supplemental Notification for 1,2-Diaminocyclohexane.

- 5. Support Information for Confidentiality Claims for 8EHQ-07-16749.
- Two sanitized copies of the Support Information for Confidentiality Claims for 8EHQ-07-16749.
- 7. Two sanitized copies of this letter.

This information is being submitted in accordance with TSCA Section 8(e) guidance. Please do not hesitate to contact me if you have any questions. I may be reached at .

Sincerely,

**Attachments** 

## **Support Information for Confidentiality Claims**

1. Is your company asserting this confidential business information (CBI) claim on its own behalf? If the answer is no, please provide company name, address and telephone number of entity asserting claim.

is asserting this CBI claim on its own behalf.

2. For what period do you assert your claim(s) of confidentiality? If the claim is to extend until a certain event or point in time, please indicate that event or time period. Explain why such information should remain confidential until such point.

The information of the study report being claimed as CBI should be held confidential indefinitely.

3. Has the information that you are claiming as confidential been disclosed to any other governmental agency, or to this Agency at any other time? Identify the Agency to which the information was disclosed and provide the date and circumstances of the same. Was the disclosure accompanied by a claim of confidentiality? If yes, attach a copy of said document reflecting the confidentiality agreement.

The report has not been disclosed to any other agency. It is possible that a robust summary of the study data, not including the information claimed as CBI, could be used in High Production Volume program submittals.

4. Briefly describe any physical or procedural restrictions within your company relating to the use and storage of the information you are claiming CBI.

Access to the building where the Study Report is housed is restricted to employees and to guests who are escorted by an employee. An electronic version of the report is stored on a password-protected data server. Access to that server requires approval from the IT department as well as the Director of Environmental, Health and Safetv.

5. If anyone outside your company has access to any of the information claimed CBI, are they restricted by confidentiality agreement(s). If so, explain the content of the agreement(s).

The entities outside who have access to the Study Report are restricted by confidentiality agreements with . These entities include the performing laboratory itself, a 3<sup>rd</sup> party consultant under contract to to assist with the final data review and outside legal counsel which provides legal assistance and review of any submissions to a government agency.

's contract with the testing laboratory states:

All Studies, Study Protocols and other information developed for by Laboratory in connection with the Work performed hereunder, the existence and conduct of any

discussion between the Parties, and the terms of this Agreement, shall also constitute Confidential Information . . . 's Confidential Information shall be held in strictest confidence by Laboratory and shall be used solely for purposes of performing the Work. Laboratory shall not disclose any of 's Confidential Information to anyone...

's Services Agreement with the 3rd party consultant states:

The consultant shall "hold 's Proprietary Information in strictest confidence, shall not disclose it to others, shall use it solely for purposes of performing such Service, and shall upon 's request, deliver to or destroy Proprietary Information ...."

- 6. Does the information claimed as confidential appear or is it referred to in any of the following:
  - a. Advertising or promotional material for the chemical substance or the resulting and product;
  - b. Material safety data sheets or other similar materials (such as technical data sheets) for the substance or resulting end product (include copies of this information as it appears when accompanying the substance and/or product at the time of transfer or sale);
  - c. Professional or trade publications; or
  - d. Any other media or publications available to the public or to your competitors. If you answered yes to any of the above, indicate where the information appears, include copies, and explain why it should nonetheless be treated as confidential.

While the *results* of the study will appear on Material Safety Data Sheets, the information claimed as confidential does not and will not appear in any of the materials listed above.

7. Has EPA, another federal agency, or court made any confidentiality determination regarding information associated with this substance? If so, provide copies of such determinations.

No.

8. Describe the substantial harmful effects that would result to your competitive position if the CBI information is made available to the public? In your answer, explain the causal relationship between disclosure and any resulting substantial harmful effects. Consider in your answer such constraints as capital and marketing cost, specialized technical expertise, or unusual processes and your competitors access to your customers. Address each piece of information claimed CBI separately.

A competitor, upon having easily obtainable access to the association between the company, the commercial product name identified in the study and the study details could use this information to their commercial advantage in an attempt to position an alternative to the product in the marketplace.

9. Has the substance been patented in the U.S. or elsewhere? Is a patent for the substance currently pending?

No patent application has been filed for this substance.

- 10. Is this substance/product commercially available and if so, for how long has it been available on the commercial market?
  - a. If on the commercial market, are your competitors aware that the substance is commercially available in the U.S.?
  - b. If not already commercially available, describe what stage of research and development (R&D) the substance is in, and estimate bow soon a market will be established.
  - c. What is the substance used for and what type of product(s) does it appear in.

is currently sold in the US and the EU as an intermediate for use in manufacture of curing agents for epoxy resins and chain extenders for polyurethanes. has been on the commercial market for approximately 20 years. Competitors would be aware that the substance is commercially available.

11. Describe whether a competitor could employ reverse engineering to identically recreate the substance?

Yes.

- 12. Do you assert that disclosure of this information you are claiming CBI would reveal:
  - a. confidential processes used in manufacturing the substance;

No

- b. if a mixture, the actual portions of the substance in the mixture; or
- c. information unrelated to the effects of the substance on human health or the environment?

Yes

If your answer to any of the above questions is yes, explain how such information would be revealed.

It would reveal the company name, the commercial product name and the testing laboratory associated with the preliminary test report data being submitted for the chemical substance.

13. Provide the Chemical Abstract Service Registry Number for the product, if known. Is your company applying for a CAS number now or in the near future? If you have applied for a CAS number, include a copy of the contract with CAS.

The CAS Registry Number is 694-83-7.

14. Is the substance or any information claimed CBI the subject of FIFRA regulation or reporting? If so, explain.

No.

### Public Version

TRACKING Numb. TSCA Document Control Office (7407M) ATTN: TSCA Section 8(e) Coordinator EPA East Building, Room 6428 Office of Pollution Prevention and Toxics U.S. Environmental Protection Agency 1201 Constitution Avenue, NW Washington, DC 20460-0001 TSCA 8(e) Submission for draft Sub-chronic Toxicity data on 1,2-Diaminocyclohexane Dear Sir: is submitting draft results from an OECD 422, sub-chronic toxicity study on 1,2-CASRN 694-83-7, Diaminocyclohexane ( Gross pathology results from a 28-day toxicity study with in drinking water, revealed a pale discoloration of livers in male rats of the high dose group (500 mg/kg). Pale discoloration of the liver was noted in 5 males. No discoloration was seen in any other dose group (0, 50, 150 mg/kg). No clear effect on liver weight was noted when compared to other high dose male animals which did not show pale discoloration of the liver. However, when adjusted for body weight, an increase in liver weight was noted in all high dose males, when compared to control males. The NOEL for liver effects was 150 mg/kg. In order to further evaluate whether the pale discoloration and/or organ weight changes are of toxicological relevance, microscopic examination and evaluation will be conducted. In the absence of microscopic information there is an indication that there may be a treatment related effect on the liver in the high dose male rats. The above information is from a draft study that has not yet been completed. \[ \] will submit the final version of the study to EPA when it becomes available. This report is being submitted in accordance with TSCA Section 8(e) guidance. Please do not hesitate to contact me if you have any questions. I may be reached at Sincerely, Attachments





### MACROSCOPIC FINDINGS MALES ALL NECROPSIES

ANIMAL ORGAN		FINDING	DAY OF DEATH							
GROU	GROUP 1 (CONTROL)									
1	•	No findings noted	Scheduled necropsy, 08Feb2007							
2		No findings noted	Scheduled necropsy, 08Feb2007							
3		No findings noted	Scheduled necropsy, 08Feb2007							
4		No findings noted	Scheduled necropsy, 08Feb2007							
5	Kidneys	Right side: pelvic dilation.	Scheduled necropsy, 08Feb2007							
6	Bone	Tail apex: bent.	Scheduled necropsy, 08Feb2007							
7		No findings noted	Scheduled necropsy, 08Feb2007							
8		No findings noted	Scheduled necropsy, 08Feb2007							
9		No findings noted	Scheduled necropsy, 08Feb2007							
10		No findings noted	Scheduled necropsy, 08Feb2007							
	P 2 (50 MG/KG)									
11		No findings noted	Scheduled necropsy, 08Feb2007							
12		No findings noted	Scheduled necropsy, 08Feb2007							
13		No findings noted	Scheduled necropsy, 08Feb2007							
14	_	No findings noted	Scheduled necropsy, 08Feb2007							
15	Bone	Tail apex: bent.	Scheduled necropsy, 08Feb2007							
16		No findings noted	Scheduled necropsy, 08Feb2007							
17		No findings noted	Scheduled necropsy, 08Feb2007							
18		No findings noted	Scheduled necropsy, 08Feb2007							
19		No findings noted	Scheduled necropsy, 08Feb2007							
20	Seminal vesicles	Right side: reduced in size.	Scheduled necropsy, 08Feb2007							
GROU	P 3 (150 MG/KG)									
21	,	No findings noted	Scheduled necropsy, 08Feb2007							
22		No findings noted	Scheduled necropsy, 08Feb2007							
23		No findings noted	Scheduled necropsy, 08Feb2007							
24		No findings noted	Scheduled necropsy, 08Feb2007							
25		No findings noted	Scheduled necropsy, 08Feb2007							
26		No findings noted	Scheduled necropsy, 08Feb2007							
27		No findings noted	Scheduled necropsy, 08Feb2007							
28		No findings noted	Scheduled necropsy, 08Feb2007							
29		No findings noted	Scheduled necropsy, 08Feb2007							
30	Seminal vesicles	Left side: reduced in size.	Scheduled necropsy, 08Feb2007							
	P 4 (500 MG/KG)									
31	Liver	Discolouration, pale.	Scheduled necropsy, 08Feb2007							
32		No findings noted	Scheduled necropsy, 08Feb2007							
33	Liver	Discolouration, pale.	Scheduled necropsy, 08Feb2007							
34	Character and the control of the con	No findings noted	Scheduled necropsy, 08Feb2007							
35	Liver	Discolouration, pale.	Scheduled necropsy, 08Feb2007							
36	Liver	Discolouration, pale.	Scheduled necropsy, 08Feb2007							
37		No findings noted	Scheduled necropsy, 08Feb2007							
38		No findings noted	Scheduled necropsy, 08Feb2007							
39	Liver	No findings noted	Scheduled necropsy, 08Feb2007							
40	Liver	Discolouration, pale.	Scheduled necropsy, 08Feb2007							







ANIMAL	BODY W. (GRAM)	BRAIN (GRAM)	HEART (GRAM)	LIVER (GRAM)	THYMUS (GRAM)
GROUP 1	(CONTROL)				
1	451	2.03	1.348	12.08	0.619
2	413	2.02	1.319	10.65	0.324
3	444				
4	410	1.89	1.149	9.95	0.417
5	421				
6	437	2.13	1.240	11.73	0.532
7	451	2.14	1.259	12.94	0.445
8	397				
9	380				
10	437				
GROUP 2	(50 MG/KG)				
11	453				
12	407	2.21	1.273	10.47	0.334
13	410	2.03	1.285	10.75	0.338
14	420	2.13	1.257	10.65	0.369
15	381				
16	395	2.20	1.405	10.41	0.450
17	410	2.11	1.391	9.82	0.269
18	408				
19	422				
20	458				~~~
GROUP 3	(150 MG/KG)			•	
21	411	2.25	1.389	11.26	0.405
22	459	2.11	1.490	11.30	0.556
23	375	1.95	1.212	9.74	0.236
24	386	2.11	1.203	9.23	0.311
25	464	2.01	1.447	13.12	0.386
26	400			~~-	
27	455				
28	425				
29	396				
30	388		****		<del></del>
GROUP 4	(500 MG/KG)				
31	412	2.15	1.405	12.49	0.242
32	410	2.11	1.380	11.50	0.347
33	410				
34	408	2.07	1.453	12.90	0.284
35	381	2.06	1.446	12.98	0.305
36	384	2.08	1.398	12.44	0.248
37	391				
38	411				
39	393				
40	428		allen spin lengt		

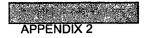






ANIMAL	KIDNEYS (GRAM)	ADRENALS (GRAM)	SPLEEN (GRAM)	TESTES (GRAM)	EPIDIDYMIDES (GRAM)
GROUP 1	(CONTROL)				
1	3.00	0.068	1.052	3.48	1.054
2	3.29	0.070	1.096	4.51	1.448
3				4.10	1.357
4	2.82	0.068	0.781	3.83	1.167
5				4.34	1.224
6	3.17	0.046	1.219	3.92	1.181
7	3.50	0.045	1.250	4.01	
8	5.50	0.000	1.230		1.229
9		<del></del>		4.10	1.142
10		<b></b>		3.86	1.344
łU	<b></b>			4.25	1.353
	(50 MG/KG)				
11				3.66	1.351
12	3.20	0.067	0.937	4.14	1.187
13	2.93	0.073	0.938	3.79	1.150
14	2.96	0.087	0.841	3.70	1.262
15				3.62	1.209
16	3.00	0.058	1.086	3.60	1.290
17	3.54	0.066	0.816	3.01	1.024
18				3.72	1.284
19				3.92	1.313
20				3.78	1.199
GROUP 3	(150 MG/KG)				
21	2.82	0.076	1.072	3.58	1.182
22	3.63	0.064	1.084	4.18	1.248
23	2.96	0.059	0.846	3.64	1.124
24	2.88	0.079	0.889	3.49	1.163
25	3.19	0.074	1.223	4.30	1.242
26	3.19	0.074	1.223	3.86	1.242
27				3.69	1.074
28				3.79	
29					1.176
30				4.21 3.70	1.166 1.158
	(500 MG/KG)				
31	3.19	0.085	0.866	3.74	1.013
32	3.13	0.082	1.013	3.99	0.909
33				3.97	1.058
34	3.48	0.085	0.913	4.22	1.032
35	3.09	0.076	0.835	3.58	1.021
36	2.88	0.062	0.820	3.83	0.995
37				3.87	0.886
38				4.57	1.148
39				3.84	1.172
40				4.35	1.124







ANIMAL	BODY W. (GRAM)	BRAIN (%)	HEART (%)	LIVER (%)	THYMUS (%)	
GROUP 1	(CONTROL)					
1	` 451	0.45	0.299	2.68	0.137	
2	413	0.49	0.319	2.58	0.078	
3	444					
4	410	0.46	0.280	2.43	0.102	
5	421					
6	437	0.49	0.284	2.68	0.122	
7	451	0.47	0.279	2.87	0.099	
8	397					
9	380					
10	437					
GROUP 2	(50 MG/KG)					
11	453					
12	407	0.54	0.313	2.57	0.082	
13	410	0.49	0.313	2.62	0.082	
14	420	0.51	0.299	2.53	0.088	
15	381					
16	395	0.56	0.356	2.63	0.114	
17	410	0.51	0.339	2.39	0.066	
18	408					
19	422					
20	458					
GROUP 3	(150 MG/KG)					
21	411	0.55	0.338	2.74	0.099	
22	459	0.46	0.325	2.46	0.121	
23	375	0.52	0.323	2.60	0.063	
24	386	0.55	0.312	2.39	0.081	
25	464	0.43	0.312	2.83	0.083	
26	400					
27	455					
28	425					
29	396					
30	388					
GROUP 4	(500 MG/KG)					
31	412	0.52	0.341	3.03	0.059	
32	410	0.51	0.337	2.80	0.085	
33	410					
34	408	0.51	0.356	3.16	0.070	
35	381	0.54	0.380	3.41	0.080	
36	384	0.54	0.364	3.24	0.065	
37	391					
38	411					
39	393					
40	428					

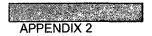


APPENDIX 2

ANIMAL	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	TESTES (%)	EPIDIDYMIDES (%)
GROUP 1	(CONTROL)				
1	0.66	0.015	0.233	0.77	0.234
2	0.80	0.017	0.265	1.09	0.351
3				0.92	0.306
4	0.69	0.017	0.190	0.93	0.285
5				1.03	0.291
6	0.72	0.011	0.279	0.90	0.270
7	0.78	0.019	0.277	0.89	0.273
8				1.03	0.288
9				1.02	0.354
10				0.97	0.310
-				0.57	0.010
	(50 MG/KG)			0.04	0.000
11	0.70	0.046	0.230	0.81	0.298
12	0.79	0.016		1.02	0.292
13	0.71	0.018	0.229	0.93	0.280
14	0.70	0.021	0.200	0.88	0.300
15				0.95	0.317
16	0.76	0.015	0.275	0.91	0.327
17	0. <b>86</b>	0.016	0.199	0.73	0.250
18				0.91	0.315
19				0.93	0.311
20				0.83	0.262
GROUP 3	(150 MG/KG)				
21	0.69	0.018	0.261	0.87	0.288
22	0.79	0.014	0.236	0.91	0.272
23	0.79	0.016	0.226	0.97	0.300
24	0.75	0.020	0.230	0.90	0.301
25	0.69	0.016	0.264	0.93	0.268
26		,		0.97	0.269
27				0.81	0.254
28		<b>~</b>		0.89	0.277
29				1.06	0.294
30				0.95	0.298
GROUD 4	(500 MG/KG)				
31	0.77	0.021	0.210	0.91	0.246
32	0.76	0.021	0.247	0.97	0.222
32 33	0.70 <del></del>	0.020		0.97	0.258
33 34	0.85	0.021	0.224	1.04	0.253
		0.021	0.219	0.94	0.268
35 36	0.81	0.020	0.214	1.00	0.259
36 37	0.75	0.010	U.2 14	0.99	0.239
37 20				0.9 <del>9</del> 1.11	0.227
38					0.279
39				0.98	
40				1.02	0.263

## Public Version

	TRACKING Numb
(	
	TSCA Document Control Office (7407M) ATTN: TSCA Section 8(e) Coordinator EPA East Building, Room 6428 Office of Pollution Prevention and Toxics U.S. Environmental Protection Agency 1201 Constitution Avenue, NW Washington, DC 20460-0001
	Re: TSCA 8(e) Submission for draft Sub-chronic Toxicity data on 1,2-Diaminocyclohexane
	Dear Sir:
1	Is submitting draft results from an OECD 422, sub-chronic toxicity study on 1,2- Diaminocyclohexane ( CASRN 694-83-7, K
	Gross pathology results from a 28-day toxicity study with in drinking water, revealed pale discoloration of livers in male rats of the high dose group (500 mg/kg). Pale discoloration of the livers noted in 5 males. No discoloration was seen in any other dose group (0, 50, 150 mg/kg). No clear effect on liver weight was noted when compared to other high dose male animals which did not show pale discoloration of the liver. However, when adjusted for body weight, an increase in liver weight was noted in all high dose males, when compared to control males. The NOEL for liver effects was 150 mg/kg.
	In order to further evaluate whether the pale discoloration and/or organ weight changes are of toxicological relevance, microscopic examination and evaluation will be conducted. In the absence of microscopic information there is an indication that there may be a treatment related effect on the liver the high dose male rats.
	The above information is from a draft study that has not yet been completed. [ ] will submit the final version of the study to EPA when it becomes available.
	This report is being submitted in accordance with TSCA Section 8(e) guidance. Please do not hesitate to contact me if you have any questions. I may be reached at
	Sincerely,
	Attachments





### MACROSCOPIC FINDINGS MALES ALL NECROPSIES

ANIM	AL ORGAN	FINDING	DAY OF DEATH
GROU	JP 1 (CONTROL)		
1	,	No findings noted	Scheduled necropsy, 08Feb2007
2		No findings noted	Scheduled necropsy, 08Feb2007
3		No findings noted	Scheduled necropsy, 08Feb2007
4		No findings noted	Scheduled necropsy, 08Feb2007
5	Kidneys	Right side: pelvic dilation.	Scheduled necropsy, 08Feb2007
6	Bone	Tail apex: bent.	Scheduled necropsy, 08Feb2007
7		No findings noted	Scheduled necropsy, 08Feb2007
8		No findings noted	Scheduled necropsy, 08Feb2007
9		No findings noted	Scheduled necropsy, 08Feb2007
10		No findings noted	Scheduled necropsy, 08Feb2007
GROU	JP 2 (50 MG/KG)		
11	·	No findings noted	Scheduled necropsy, 08Feb2007
12		No findings noted	Scheduled necropsy, 08Feb2007
13		No findings noted	Scheduled necropsy, 08Feb2007
14		No findings noted	Scheduled necropsy, 08Feb2007
15	Bone	Tail apex: bent.	Scheduled necropsy, 08Feb2007
16		No findings noted	Scheduled necropsy, 08Feb2007
17		No findings noted	Scheduled necropsy, 08Feb2007
18		No findings noted	Scheduled necropsy, 08Feb2007
19		No findings noted	Scheduled necropsy, 08Feb2007
20	Seminal vesicles	Right side: reduced in size.	Scheduled necropsy, 08Feb2007
	JP 3 (150 MG/KG)		
21		No findings noted	Scheduled necropsy, 08Feb2007
22		No findings noted	Scheduled necropsy, 08Feb2007
23		No findings noted	Scheduled necropsy, 08Feb2007
24		No findings noted	Scheduled necropsy, 08Feb2007
25		No findings noted	Scheduled necropsy, 08Feb2007
26		No findings noted	Scheduled necropsy, 08Feb2007
27		No findings noted	Scheduled necropsy, 08Feb2007
28		No findings noted	Scheduled necropsy, 08Feb2007
29		No findings noted	Scheduled necropsy, 08Feb2007
30	Seminal vesicles	Left side: reduced in size.	Scheduled necropsy, 08Feb2007
	JP 4 (500 MG/KG)	min to the second	Out and also discussed a OOF 1 0007
31	Liver	Discolouration, pale.	Scheduled necropsy, 08Feb2007
32		No findings noted	Scheduled necropsy, 08Feb2007
33	Liver	Discolouration, pale.	Scheduled necropsy, 08Feb2007
34		No findings noted	Scheduled necropsy, 08Feb2007
35	Liver	Discolouration, pale.	Scheduled necropsy, 08Feb2007
36	Liver	Discolouration, pale.	Scheduled necropsy, 08Feb2007
37		No findings noted	Scheduled necropsy, 08Feb2007
38		No findings noted	Scheduled necropsy, 08Feb2007
39	4.	No findings noted	Scheduled necropsy, 08Feb2007
40	Liver	Discolouration, pale.	Scheduled necropsy, 08Feb2007





ANIMAL	BODY W. (GRAM)	BRAIN (GRAM)	HEART (GRAM)	LIVER (GRAM)	THYMUS (GRAM)	
GROUP 1	(CONTROL)					
1	` 451	2.03	1.348	12.08	0.619	
2	413	2.02	1.319	10.65	0.324	
3	444					
4	410	1.89	1.149	9.95	0.417	
5	421					
6	437	2.13	1.240	11.73	0.532	
7	451	2.14	1.259	12.94	0.445	
8	397					
9	380					
10	437				***	
CPOUR 2	(50 MG/KG)					
11	453					
12	407	2.21	1.273	10.47	0.334	
13	410	2.03	1.285	10.75	0.338	
14	420	2.13	1.257	10.65	0.369	
15	381			70.00		
16	395	2.20	1.405	10.41	0.450	
17	410	2.11	1.391	9.82	0.269	
18	408					
19	422					
20	458					
CPOUR 3	(150 MG/KG)					
21	411	2.25	1.389	11.26	0.405	
22	459	2.11	1.490	11.30	0.556	
23	375	1.95	1.212	9.74	0.236	
24	386	2.11	1.203	9.23	0.311	
25	464	2.01	1.447	13.12	0.386	
26	400					
27	455					
28	425					
29	396					
30	388					
GPOUP 4	(500 MG/KG)					
31	412	2.15	1.405	12.49	0.242	
32	410	2.11	1.380	11.50	0.347	
33	410	Z.11 =~~			0.041	
34	408	2.07	1.453	12.90	0.284	
35	381	2.06	1.446	12.98	0.305	
36	384	2.08	1.398	12.44	0.248	
37	391					
38	411					
39	393					
40	428					
. •						







ANIMAL	KIDNEYS (GRAM)	ADRENALS (GRAM)	SPLEEN (GRAM)	TESTES (GRAM)	EPIDIDYMIDES (GRAM)
GROUP 1	(CONTROL)				
1	3.00	0.068	1.052	3.48	1.054
2	3.29	0.070	1.096	4.51	1. <del>44</del> 8
3				4.10	1.357
4	2.82	0.068	0.781	3.83	1.167
5				4.34	1.224
6	3.17	0.046	1.219	3.92	1.181
7	3.50	0.085	1.250	4.01	1.229
8				4.10	1.142
9				3.86	1.344
10				4.25	1.353
GROUP 2	(50 MG/KG)				
11				3.66	1.351
12	3.20	0.067	0.937	4.14	1.187
13	2.93	0.073	0.938	3.79	1.150
14	2.96	0.087	0.841	3.70	1.262
15				3.62	1.209
16	3.00	0.058	1.086	3.60	1.290
17	3.54	0.066	0.816	3.01	1.024
18				3.72	1.284
19				3.92	1.313
20			_~-	3.78	1.199
GROUP 3	(150 MG/KG)				
21	2.82	0.076	1.072	3.58	1.182
22	3.63	0.064	1.084	4.18	1.248
23	2.96	0.059	0.846	3.64	1.124
24	2.88	0.079	0.889	3.49	1.163
25	3.19	0.074	1.223	4.30	1.242
26				3.86	1.074
27				3.69	1.157
28				3.79	1.176
29				4.21	1.166
30				3.70	1.158
<b>GROUP 4</b>	(500 MG/KG)				
31	3.19	0.085	0.866	3.74	1.013
32	3.13	0.082	1.013	3.99	0.909
33				3.97	1.058
34	3.48	0.085	0.913	4.22	1.032
35	3.09	0.076	0.835	3.58	1.021
36	2.88	0.062	0.820	3.83	0.995
37				3.87	0.886
38				4.57	1.148
39				3.84	1.172
40				4.35	1.124







ANIMAL	BODY W. (GRAM)	BRAIN (%)	HEART (%)	LIVER (%)	THYMUS (%)	
GROUP 1	(CONTROL)					
1	451	0.45	0.299	2.68	0.137	
2	413	0.49	0.319	2.58	0.078	
3	444					
4	410	0.46	0.280	2.43	0.102	
5	421					
6	437	0.49	0.284	2.68	0.122	
7	451	0.47	0.279	2.87	0.099	
8	397					
9	380					
10	437					
CDOUB 2	(FO MO(VC)					
11	( <b>50 MG/KG)</b> 453		MA (M. 404			
12	407	0.54	0.313	2.57	0.082	
13	410	0.49	0.313	2.62		
			0.299	2.52 2.53	0.082	
14	420	0.51	0.299	2.53	0.088	
15	381					
16	395	0.56	0.356	2.63	0.114	
17	410	0.51	0.339	2.39	0.066	
18	408				~	
19	422					
20	458					
	(150 MG/KG)					
21	411	0.55	0.338	2.74	0.099	
22	459	0.46	0.325	2.46	0.121	
23	375	0.52	0.323	2.60	0.063	
24	386	0.55	0.312	2.39	0.081	
25	464	0.43	0.312	2.83	0.083	
26	400				<del></del>	
27	455					
28	425					
29	396					
30	388			**-		
GROUP 4	(500 MG/KG)					
31	412	0.52	0.341	3.03	0.059	
32	410	0.51	0.337	2.80	0.085	
33	410					
34	408	0.51	0.356	3.16	0.070	
35	381	0.54	0.380	3.41	0.080	
36	384	0.54	0.364	3.24	0.065	
37	391					
38	411					
39	393					
40	428					



APPENDIX 2

ANIMAL	KIDNEYS (%)	ADRENALS (%)	SPLEEN (%)	TESTES (%)	EPIDIDYMIDES (%)
GROUP 1	(CONTROL)				
1	0.66	0.015	0.233	0.77	0.234
2	0.80	0.017	0.265	1.09	0.351
3				0.92	0.306
4	0.69	0.017	0.190	0.93	0.285
5				1.03	0.291
6	0.72	0.011	0.279	0.90	0.270
7	0.78	0.019	0.277	0.89	0.273
8				1.03	0.288
9				1.02	0.354
10				0.97	0.310
GROUP 2	(50 MG/KG)				
11				0.81	0.298
12	0.79	0.016	0.230	1.02	0.292
13	0.71	0.018	0.229	0.93	0.280
14	0.70	0.021	0.200	0.88	0.300
15				0.95	0.317
16	0.76	0.015	0.275	0.91	0.327
17	0.86	0.016	0.199	0.73	0.250
18				0.91	0.315
19				0.93	0.311
20				0.83	0.262
	(150 MG/KG)				
21	0.69	0.018	0.261	0.87	0.288
22	0.79	0.014	0.236	0.91	0.272
23	0.79	0.016	0.226	0.97	0.300
24	0.75	0.020	0.230	0.90	0.301
25	0.69	0.016	0.264	0.93	0.268
26		,		0.97	0.269
27				0.81	0.254
28				0.89	0.277
29				1.06	0.294
30				0.95	0.298
	(500 MG/KG)				
31	0.77	0.021	0.210	0.91	0.246
32	0.76	0.020	0.247	0.97	0.222
33				0.97	0.258
34	0.85	0.021	0.224	1.04	0.253
35	0.81	0.020	0.219	0.94	0.268
36	0.75	0.016	0.214	1.00	0.259
37				0.99	0.227
38				1.11	0.279
39				0.98	0.298
40				1.02	0.263